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Research Article

The Effect of Body Mass Index on the Diagnostic Yield of Endobronchial Ultrasound Guided Transbronchial Needle Aspiration of Hilar-Mediastinal Lymphadenopathy and Masses

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Abstract

Background: The prevalence of obesity is increasing and has reached epidemic proportions in some countries. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) offers a minimally invasive option for sampling hilar and mediastinal lymph nodes (LN) and masses. An excess of mediastinal adiposity in obese patients can result in significant mediastinal widening and can potentially interfere with sampling of lymph nodes and masses. This study explored whether body mass index (BMI) influences the diagnostic yield of EBUS-guided TBNA when evaluating intrathoracic LN or masses.

Methods: We performed a retrospective review involving a cohort of 240 consecutive patients who underwent EBUS-guided TBNA for enlarged intrathoracic lymph nodes or masses. Procedures occurred between January 2011-January 2014 at a single teaching community medical center. Subjects were grouped based on their BMI (Group 1: BMI < 30, Group 2: BMI 30 - 39, and Group 3: BMI ≥ 40). Positive diagnostic yield was defined as either a definitive diagnosis or the presence of lymphocytes on the biopsy specimen in the assessment of intrathoracic lymphadenopathy and masses. The primary outcome was the proportion of patients in each BMI group with a positive diagnostic yield of EBUS- TBNA; 95% binomial confidence intervals (CI) were calculated and the difference in diagnostic yield among groups was compared using a two-sided chi-square test with alpha = 0.05. Secondary outcomes included the risks in each BMI group of procedural complications and mediastinoscopy following a non-diagnostic EBUS- guided TBNA.

Results: A total of 374 lymph node stations and 61 masses were sampled in 240 patients. The average positive diagnostic yield across all groups in our study was 93%, consistent with the overall diagnostic yield of EBUS-TBNA reported in the literature (88-96%). There was no significant difference in diagnostic yield amongst the 3 groups. Two pneumothoraces occurred in the setting of additional transbronchial biopsy performance during EBUS-TBNA (0.83%). One was managed conservatively with serial imaging and the other required needle aspiration (both in Group 1). Four patients (1.7%) were admitted due to respiratory failure post-procedure (Groups 1 and 2). Mediastinoscopy was performed in ten (10) patients (4.2%), of which 6 (60%) had a definitive diagnosis (half of them in Group 1).

Conclusion: Tissue sampling is generally indicated for enlarged hilar and mediastinal lymph nodes or intrathoracic masses on CT scan of the chest and/or metabolically active on positron emission tomography (PET) imaging in a wide range of clinical contexts. We found that BMI does not affect the diagnostic yield of EBUS-guided TBNA of intrathoracic lymphadenopathy or masses.

Keywords: *Body Mass Index; Endobronchial Ultrasound Guided Transbronchial Needle; Aspiration; Hilar*

Abbreviations

BMI: Body Mass Index; BOOP: Bronchiolitis Obliterans Organizing Pneumonia; CT: Computer Tomography; CI: Confidence Interval; CTSI: Clinical and Translational Science Institute-Tufts; DLBCL: Diffuse Large B-cell Lymphoma; EBUS: Endobronchial Ultrasound; L: Left; LCC: Large Cell Carcinoma; LN: Lymph Node; NSCLC: Non-Small Cell Lung Cancer; PET: Positron Emission Tomography; R: Right; ROSE: Rapid On-site Histopathologic Evaluation; SCLC: Small Cell Lung Cancer; STD: Standard Deviation; SCC: Squamous Cell Carcinoma; TBNA: Transbronchial Needle Aspiration

Introduction

Obesity is a major problem in the United States and a growing concern around the world. The prevalence of obesity is increasing and has reached epidemic proportions in some countries [1]. In simple obesity, excessive fat is generally stored at various body sites, notably in the mediastinum, subcutaneous tissue, omentum, mesentery, and perirenal tissue. Mediastinal fat deposition is a benign condition, which rarely causes severe consequences. Although excessive fatty tissue deposition may be present within the mediastinum in obese persons, an amount of fat sufficient to produce significant mediastinal widening on the chest roentgenogram though rare, can occur [2].

Mediastinal abnormalities can present a challenging differential diagnosis. Mediastinal widening has been evaluated by routine chest radiography, conventional tomography, and computed tomography in patients with simple obesity. Computed tomography was the only modality that definitively diagnosed mediastinal increased fat deposition [3,4].

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) offers a minimally invasive option for sampling hilar and mediastinal lymph nodes (LN) and masses [5,6]. EBUS-guided TBNA is now considered a standard procedure worldwide, used in combination with flexible bronchoscopy to obtain biopsies of undiagnosed intrathoracic lymph nodes and masses [7]. EBUS also provides structural characteristics of the airway wall and adjacent tissues.

Medical ultrasonography uses ultrasound waves to create images of the body for diagnostic purposes and to guide procedures. Nevertheless, whether one is imaging the abdomen, heart, lung or pleura, the physical principles of ultrasonography are the same. The piezoelectric crystals in the transducer send out a brief pulse of strong high-frequency sound waves that penetrate the body tissue. The sound waves are reflected back to the transducer, which serves as the sensor and the source of signal. The acoustic impedance of the adjacent tissue determines the degree of reflection. Acoustic impedance is related largely to tissue density, although the propagation velocity of sound through different tissues of varied densities is a factor. Ultrasound waves undergo refraction, scattering and attenuation as they pass through tissues of different densities, all of which degrade and alter image quality on examining deeper structures [8].

An excess of mediastinal adiposity in obese patients can result in significant mediastinal widening and can potentially interfere with sampling of lymph nodes and masses. This study explored whether obesity influences the diagnostic yield of EBUS-guided TBNA when evaluating enlarged intrathoracic lymph nodes or masses. To the best of our knowledge this is the first review looking at patients undergoing EBUS-guided TBNA with respect to their body-mass index (BMI) and their diagnostic yield.

Materials and Methods

Study design

This single-center study employed a retrospective observational design. The waiver of consent authorization and protocol was approved by the institutional review board (IRB) of St. Elizabeth Medical Center, Boston, for a period of 1 year.

A cohort of 240 consecutive patients who underwent EBUS-guided TBNA with undiagnosed intrathoracic lymphadenopathy or mass was identified using the international classification of diseases (ICD-9) codes obtained from the billing department of our hospital. Pathological hilar and mediastinal lymph nodes and masses of short axis ≥ 5 mm confirmed on CT scan of the chest are routinely considered for biopsy. At our facility, we perform 2 - 4 passes per lymph node station on average [9].

Study Method

The procedures occurred between January 2011- January 2014 at a single teaching community medical center. EBUS-guided TBNA bronchoscope (BF-UC180F; Olympus, Tokyo, Japan) is used in our facility for the performance of procedure. Rapid on-site histopathologic evaluation (ROSE) was not performed in any of the samples taken. Subjects were grouped based on their body mass index (Group 1: BMI < 30, Group 2: BMI 30 - 39, and Group 3: BMI ≥ 40).

Positive diagnostic yield was defined as either a definitive diagnosis or the presence of lymphocytes on the biopsy specimen in the assessment of intrathoracic lymphadenopathy and masses. The primary outcome was the proportion of patients in each BMI group with a positive diagnostic yield of EBUS-guided TBNA; 95% confidence intervals (CI) were calculated for each proportion and the difference among groups was compared using a two-sided chi-square test with alpha = 0.05.

Secondary outcomes included the risks in each BMI group of procedural complications (including pneumothorax, respiratory decompensation, hemodynamic instability, significant bleeding requiring interventions, cardiac arrhythmias and mediastinoscopy following a non-diagnostic EBUS-guided TBNA.

Results

A total of 374 lymph node stations and 61 masses were sampled in 240 patients with a mean age of 64.4 ± 14.2 years (range, 25 - 92) with almost equal distribution of both males and females: 121 and 119 respectively (Table 1).

BMI Groups	Mean Age ± STD	Female gender (%)	LAD (n = 374)	MASSES (n = 61)
< 30 (n = 150)	65.3 ± 14.8	73 (48.7)	223	42
> 30 - 39 (n = 71)	64.4 ± 12.7	36 (52.1)	110	18
> 40 (n = 19)	57.9 ± 14.1	10 (52.6)	41	1

Table 1: *Demographics (Need average ages for each group).*

BMI: Body Mass Index; LAD: Lymphadenopathy; STD: Standard Deviation

A breakdown of individual lymph node stations sampled across the three BMI groups is shown in table 2. The majority of the lymph nodes were sampled from station 7 (subcarinal station). This was followed by the lower paratracheal lymph nodes (station 4R/4L) and interlobar lymph nodes at station 10R/10L. No lymph node was sampled from the left lobar station 12L or left upper paratracheal station (2L).

Masses	12L	11L	10L	4L	2L	7	2R	4R	10R	11R	12R
61	0	42	4	49	0	130	5	76	13	51	4

Table 2: *Individual Lymph node stations/Masses sampled.*

L: Left; R: Right

The average positive diagnostic yield across all groups in our study was 93%, consistent with the overall diagnostic yield of EBUS-TBNA reported in the literature (88 - 96%) [10,11]. There were no significant differences in diagnostic yield amongst the 3 groups (Table 3). The wider confidence interval (CI) in patients in BMI groups 2 and 3, compared to group 1, reflects the smaller number of patients in those groups.

BMI Group	N	% Positive Diagnostic Yield	95% Confidence Interval
1 (BMI < 30)	150	93.3	88.1, 96.8
2 (BMI 30 - 39)	71	90.1	80.7, 95.9
3 (BMI ≥ 40)	19	100	82.4, 100

Table 3: *Diagnostic Yield per each BMI group.*

Table 4 depicts the individual categories of patients who had a positive diagnostic yield across all 3 BMI groups; of those with a positive diagnostic yield, normal lymph node tissues (i.e. presence of lymphocytes on biopsy) was the most common finding. Among the cancers diagnosed, adenocarcinoma of the lung was identified in 38% of the population followed by squamous cell lung cancer (33%). The majority of the metastatic lesions identified were from breast cancer (1%).

Positive Diagnosis	N = 227 (%)
Normal LN tissue	89 (39)
Adenocarcinoma (NSCLC)	36 (16)
Squamous Cell (NSCLC)	31 (14)
Large Cell (NSCLC)	6 (3)
Small Cell Lung Cancer	22 (10)
Sarcoidosis	35 (15)
Breast Cancer	3 (1)
Others (DLBCL, Colon Cancer, Neck SCC, Mycetoma)	5 (2)

Table 4: *Positive or definitive diagnostic results.*

Mediastinoscopy was performed in 10 patients (4.2%) following a non-diagnostic EBUS-guided TBNA in this subgroup of patients with a high clinical high pretest probability for a malignancy. Of the patients undergoing mediastinoscopy, 6 (60%) had a definitive diagnosis, half of whom were in group 1.

Patient	EBUS-TBNA results	Mediastinoscopy results	Additional Procedures
1	No	No	None
2	No	No	CT guided biopsy->SCC
3	Reactive LN	Reactive LN	Thoracentesis-> SCC
4	No	Sarcoidosis	None
5	No	Mantle Cell Lymphoma	None
6	No	Adenocarcinoma Lung	None
7	No	No	CT guided biopsy->BOOP
8	No	SCC	None
9	No	SCLC	None
10	No	LCC	None

Table 5: *Mediastinoscopy Results.*

(Key: No: Non-Diagnostic; SCC: Squamous Cell Carcinoma; SCLC: Small Cell Lung Cancer; LCC: Large Cell Carcinoma; BOOP: Bronchiolitis Obliterans Organizing Pneumonia)

Two pneumothoraces occurred post procedure (0.83%). Both of these patients underwent transbronchial biopsies in addition to EBUS guided-TBNA. One was managed conservatively with serial imaging and the other required needle aspiration of pneumothorax (both were in BMI Group 1). Four patients (1.7%) were admitted due to acute hypoxic respiratory failure post-procedure (2 each in BMI Groups 1 and 2 respectively) (Table 6).

	Pneumothorax	Respiratory Failure
Group 1	2	2
Group 2	0	2
Group 3	0	0

Table 6: *Complications of Procedure (EBUS-TBNA).*

There were no hemorrhages requiring a major intervention (e.g. embolization, balloon tamponade, stent bronchial blocker, double lumen intubation or selective airway intubation) across all groups. There were no cardiac arrhythmias leading to hemodynamic instability necessitating treatment.

Discussion

Lymph node sampling is generally indicated when hilar and or mediastinal lymph nodes or masses are enlarged on CT scan of the chest and/or metabolically active on positron-emission tomography (PET) imaging in a wide range of clinical contexts. The advent of EBUS-guided TBNA has revolutionized the sampling of undiagnosed intrathoracic masses and lymphadenopathy in the last two decades. EBUS- guided TBNA procedure offers a minimally invasive approach to sampling these lesions with minimal complications.

EBUS-guided TBNA when performed in experienced hands in the absence of a rapid on-site cytologic evaluation (ROSE) has a diagnostic yield that is comparable to facilities with ROSE [12]. The diagnostic yield across the three BMI groups (93%) in our study is comparable to the average yield reported in the literature [10,11].

The impact of body mass index on the yield of EBUS-guided TBNA has never been described. In our experience, there was no difference noted in diagnostic yield between the three BMI cohorts.

A limitation of our study is the small number of patients found in the BMI Group 3 population (19 patients). All data reported reflect the actual analysis of every patient included in the study between the stated time frame.

EBUS-guided TBNA is an accurate and safe tool in the assessment and diagnosis of mediastinal and hilar lymphadenopathy. Although EBUS-TBNA cannot completely replace mediastinoscopy, it has indeed reduced the number of mediastinoscopy procedures currently being performed. In most cases, EBUS-guided TBNA is the first-line procedure before mediastinoscopy.

Conclusion

In conclusion, our study found that obesity does not influence the diagnostic yield of EBUS-guided TBNA of intrathoracic lymphadenopathy or masses: however, a larger prospective multi-center trial is needed to confirm this conclusion.

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